

AMENDMENTS TO THE CLAIMS

1.-18. (Cancel)

19. A method for identifying a regulatory sequence which is affected by a feedback mechanism on alteration of synthesis or activity of a bacterial essential protein, comprising:

- i) providing a bacterial cell having a reporter gene under the control of a candidate regulatory sequence;
- ii) selecting a target essential protein which is expressed in the cell;
- iii) altering the synthesis or activity of the essential protein;
- iv) monitoring expression of the reporter gene; and
- v) determining thereby whether the candidate regulatory sequence is affected by a feedback mechanism responsive to alteration of the synthesis or activity of the essential protein.

20. A method of identifying a regulatory sequence whose activity is affected by a feedback mechanism or an alteration of the synthesis or activity of an essential bacterial protein, comprising:

- (a) monitoring expression of a bacterial gene in a bacterial host cell in the presence of normal and altered synthesis or activity of the essential protein;
- (b) identifying differential gene expression in the presence of normal and altered synthesis or activity of the essential protein; and
- (c) identifying thereby a regulatory sequence whose activity is affected by the feedback mechanism.

21. The method of claim 20, wherein step (b) comprises:

- (a) providing an array of nucleotide sequences of the nucleic acid sequences of the bacterial cell;
- (b) recovering polynucleotide material from the cells;
- (c) applying said polynucleotide material to the array; and
- (d) monitoring for hybridization of the bacterial nucleic acid material to the array.

22. The method according to claim 20, wherein step (b) comprises recovering and separating proteins from the bacterial cell and monitoring for a change in concentration of a protein in the presence of normal and altered synthesis or activity of the essential protein.

23. A method for identifying a modulator of a bacterial essential protein, comprising:

- i) providing a bacterial host cell which expresses the essential protein, wherein the cell comprises a polynucleotide construct comprising a regulatory sequence operably linked to a reporter nucleic acid sequence, wherein the regulatory sequence is associated with a feedback mechanism responsive to alteration in the synthesis or activity of the essential protein and is identified according to the method of claim 19;
- ii) contacting a test substance with the host cell; and
- iii) monitoring expression of the reporter gene to determine thereby whether said substance modulates the synthesis or activity of the essential protein.

24. The method of claim 23, wherein the essential protein is involved in cell wall synthesis, teichoic acid synthesis, DNA replication, RNA synthesis, cell division, chromosome segregation, translation or lipid synthesis.

25. The method of claim 23, wherein inhibition of the essential protein up-regulates expression of the reporter nucleic acid sequence from the regulatory sequence.

26. The method of claim 23, wherein the regulatory sequence has the activity of a promoter for the nucleic acid sequence encoding the essential protein and inhibition of the essential protein up-regulates expression from its promoter.

27. The method of claim 23, wherein the regulatory sequence has the activity of a promoter for a gene which does not encode the essential protein but which is up-regulated via the feedback mechanism in response to alterations to the synthesis or activity of the essential protein.

28. The method of claim 23, wherein the reporter gene comprises a nucleic acid sequence which is up-regulated in response to alterations in the synthesis or activity of the essential protein, and wherein step (iii) comprises monitoring for differential expression of the gene in the presence or absence of the test substance.

29. The method according to claim 23, wherein the bacterial cell is provided with a second polynucleotide construct comprising a promoter operably linked to a second reporter gene and the method further comprises monitoring expression of the second reporter gene.

30. The method of claim 23, further comprising determining whether the test substance demonstrates specific inhibition of the essential protein.

31.-36. (Cancel)